PI profile

## Robert Davies

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|  | **Dr. Robert Davies****Titles**: Professor of Statistical and Population Genomics**Location**: Department of Statistics**Department**: Department of Statistics**Group**: Davies**Webpage**: https://davieslab.github.io/ **Email**: robert.davies@stats.ox.ac.uk |

### GMS themes:

* Genome biology (genomes and genetic variation)
* Genomics of disease
* Genomic analysis (bioinformatics and statistical genetics)
* Application of genomics in the clinic (diagnostics and therapeutics)

### Research Overview

We are a research group at the University of Oxford interested in problems at the interface of statistics, genetics and medicine. We have broad interests but are particularly focused on research that can eventually contribute towards more accurate phenotype prediction using genotypes in humans.

Project areas: Statistical genetics, methods development, phasing and imputation, whole genome sequencing, polygenic risk scores

### Specific project proposals:

* ‘Investigating properties of de novo duplication or deletion detection using non-invasive prenatal testing data’

Please contact directly for further information.

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Project proposal

# **Title**: Investigating properties of de novo duplication or deletion detection using non-invasive prenatal testing data

Supervisors: Robert Davies

Wet/dry lab mix (approx): 100% dry lab

Description: During pregnancy, the blood of the mother contains cell free DNA derived both from maternal cells, and from fetal cells. By sequencing and analyzing this cell free DNA, it is possible to detect abnormal numbers of chromosomes in the fetus (aneuploidies). This process, called non-invasive prenatal testing (NIPT), is now the clinical standard of care for aneupolidy detection, and is in widespread use around the world. However, traditional use of this method cannot detect de novo sub-chromosomal abnormalities very well, as it uses the difference in counts of reads between chromosomes or regions, and these are not very precise due to the low fraction of fetal DNA in the sample and number of reads. Recently, I had a paper accepted on a method (QUILT) for low coverage imputation that can probabilistically assign reads to maternal or paternal origin. In this project, you would study how using the principle of assigning reads to their haplotypic origin (here maternal transmitted, untransmitted or paternally transmitted) and then looking for differences in the levels in between them, can facilitate sub-chromosomal aneuploidy detection. An outline for this project could be as follows. First, to set up a simulation framework, so that for sub-chromosomal event, that simulated sequencing reads could be generated. Second, to assing reads to their haplotypic background, using either truth data or by estimating it programatically (QUILT). Third, to develop a probabilistic model to determine the probability of different mutational events (normal DNA vs duplication vs deletion), conditional on the observed sequencing reads and prior probabilities. Fourth, to evaluate this model, and compare it to one where we don’t estimate what haplotypes reads come from. Time-permitting, this evaluation would be done across a variety of factors, for example different human populations, sequencing depths, different genomic regions, etc. Taken together, this project will help us determine whether assigning sequencing reads to their chromosomal backgrounds can improve de novo subchromosomal variant detection in NIPT.

### Training Opportunities: In this project you’ll develop skills in methods development, statistics, and whole genome sequencing

Background reading / references:

* Liu Siyang, …, 2018. Genomic Analyses from Non-invasive Prenatal Testing Reveal Genetic Associations, Patterns of Viral Infections, and Chinese Population History. Cell. <https://doi.org/10.1016/j.cell.2018.08.016>
* Davies Robert, …, 2021. Rapid genotype imputation from sequence with reference panels . Nature Genetics. <https://www.nature.com/articles/s41588-021-00877-0>